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## Minimally invasive monitoring in patients under general anesthesia

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*Document Version*

Publisher's PDF, also known as Version of record

*Publication date:*

2015

[Link to publication in University of Groningen/UMCG research database](#)

*Citation for published version (APA):*

Vos, J. J. (2015). *Minimally invasive monitoring in patients under general anesthesia*. [Thesis fully internal (DIV), University of Groningen]. [S.n.].

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# Comparison of continuous noninvasive finger blood pressure monitoring with conventional intermittent automated arm blood pressure measurement in patients under general anaesthesia

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Modified from

*British Journal of Anaesthesia*, 2014;113: 67–74

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## Abstract

**Background.** In a majority of patients undergoing anesthesia for general surgery, mean arterial blood pressure (MAP) is only measured intermittently by arm cuff oscillometry ( $\text{MAP}_{\text{iNIBP}}$ ). In contrast, the Nexfin® device provides continuous noninvasive measurement of MAP ( $\text{MAP}_{\text{cNIBP}}$ ) using a finger cuff. We explored the agreement of  $\text{MAP}_{\text{cNIBP}}$  and  $\text{MAP}_{\text{iNIBP}}$  with the gold standard: continuous invasive MAP measurement by placement of a radial artery catheter ( $\text{MAP}_{\text{invasive}}$ ).

**Methods.** In a total of 120 patients undergoing elective general surgery and clinically requiring  $\text{MAP}_{\text{invasive}}$  measurement,  $\text{MAP}_{\text{iNIBP}}$  and  $\text{MAP}_{\text{cNIBP}}$  were measured in a 30-minute time period at an arbitrary moment during surgery with stable hemodynamics.  $\text{MAP}_{\text{iNIBP}}$  was measured every 5 minutes.

**Results.** Data of 112 patients were analyzed. Compared to  $\text{MAP}_{\text{invasive}}$ , modified Bland Altman analysis revealed a bias (SD) of 2 (9) mmHg for  $\text{MAP}_{\text{cNIBP}}$  and -2 (12) mmHg for  $\text{MAP}_{\text{iNIBP}}$ . Percentage errors for  $\text{MAP}_{\text{cNIBP}}$  and  $\text{MAP}_{\text{iNIBP}}$  were 22 and 32%, respectively.

**Conclusions.** In a hemodynamically stable phase in patients undergoing general anesthesia, the agreement with invasive mean arterial blood pressure of continuous noninvasive measurement using a finger cuff, was not inferior to the agreement of intermittent arm cuff oscillometry. Continuous measurements using a finger cuff can interchangeably be used as an alternative for intermittent arm cuff oscillometry in hemodynamically stable patients, with the advantage of beat-to-beat hemodynamic monitoring.



## Introduction

Mean arterial pressure (MAP) monitoring, along with pulse oximetric assessment of heart rate and arterial oxygen saturation, is mandatory in patients undergoing surgery, irrespective of the type of anesthesia the patient receives.<sup>1</sup> During major surgical procedures or in high-risk patients, continuous (invasive) blood pressure measurement using an indwelling arterial catheter is preferred to closely monitor “beat-to-beat” changes in MAP. In addition, this method can be regarded as the clinical “gold” standard for monitoring of MAP ( $\text{MAP}_{\text{invasive}}$ ). However, placement of an indwelling arterial catheter is prone to several complications.<sup>2,3</sup> Thus,  $\text{MAP}_{\text{invasive}}$  use is limited to patients in whom the advantage of continuous MAP measurement outweighs the risk of placement of the arterial catheter or when frequent arterial blood sampling is required.

In most cases, conventional noninvasive intermittent measurement of MAP ( $\text{MAP}_{\text{inIBP}}$ ) with an interval of 3-5 minutes is considered appropriate.<sup>1</sup> In addition, it is not considered harmful (i.e. noninvasive) and easy to perform. Nevertheless, its accuracy is dependent on appropriate positioning of the patient, correct cuff positioning and adequate cuff size, and may be impaired by patient conditions such as arrhythmia and obesity.<sup>4,5</sup>  $\text{MAP}_{\text{inIBP}}$  has been validated with the cuff placed around the upper arm; but since the upper arm may be inaccessible in some patients (due to wounds, fractures, edema, vascular access), cuff locations on calf or thigh are considered as alternative measurement sites though they decrease measurement accuracy considerably.<sup>5</sup> On top of decreased accuracy,  $\text{MAP}_{\text{inIBP}}$  does not allow continuous, “beat-to-beat” monitoring of MAP as it takes time to inflate and deflate the cuff. Moreover, because cuff deflation takes several seconds, the determined systolic and diastolic values originate from different heartbeats and may therefore give more inaccurate results in case of significant pulse pressure variation.<sup>6</sup>

The Nexfin device (Edwards Lifesciences, Irvine, USA), introduced in 2007, is based on the volume clamp method first introduced by the Czech physiologist Jan Penaz in 1967.<sup>7</sup> It allows continuous noninvasive blood pressure measurement ( $\text{MAP}_{\text{cNIBP}}$ ) using a photoplethysmograph and an inflatable cuff placed around a finger.<sup>8</sup> Based on the input from the photoplethysmograph, the cuff pressure is adjusted 1000 times per second to keep the arterial volume constant during the cardiac cycle. Thus, the artery is clamped at a diameter where the transmural pressure is zero, and therefore the cuff pressure is equal to the arterial blood pressure. This “volume clamping” allows measurement of an arterial pressure waveform. Finally, brachial arterial pressure is reconstructed from finger arterial pressure and displayed.<sup>9</sup> Multiple studies<sup>10-12</sup> have already investigated the accuracy of arterial blood pressure measurement by this device and compared it to invasively obtained measurements with various results. Yet, the vast majority of patients undergoing surgery is monitored solely using intermittent noninvasive measurements and therefore it is of interest whether  $\text{MAP}_{\text{cNIBP}}$  would be a valuable adjunct or could ultimately replace  $\text{MAP}_{\text{inIBP}}$  in the intraoperative setting.

Therefore, we explored in the current study in patients under general anesthesia, the agreement of both  $\text{MAP}_{\text{cNIBP}}$  and  $\text{MAP}_{\text{inIBP}}$  with the clinical standard of arterial blood pressure measurement:  $\text{MAP}_{\text{invasive}}$  measurement. In addition, we analyzed whether the side of the measurement (i.e. contra- or ipsilateral to invasive measurement) of the  $\text{MAP}_{\text{cNIBP}}$  finger cuff affected its accuracy.

## Methods

This observational study was approved by the local medical ethics committee (METc2011.052, University Medical Center Groningen, The Netherlands) and was registered at clinicaltrials.gov (NCT: 01362335).

A total of 120 patients, scheduled for elective abdominal, neurosurgical, oncological and vascular surgery under general anesthesia in and for which placement of a radial artery catheter was required on clinical grounds, were included (figure 1). Measurements took place at an arbitrary moment of stable hemodynamic conditions during surgery with a total measurement period of 30 minutes. At least 24 hours after the operation, written informed consent was obtained for analysis of the recorded data and patients were included for data-analysis.

In all patients, anesthesia was induced with propofol and sufentanil or remifentanil. Anesthesia was maintained with propofol or sevoflurane, in combination with either sufentanil or remifentanil as clinically required. Prior to data recording, a radial artery was cannulated using a 20G catheter and connected with a disposable pressure transducer (Truwave PX-600F, Edwards Lifesciences LLC, Irvine, USA).  $MAP_{iNIBP}$  was measured using cuff oscillometry at the upper arm according to routine clinical practice with the cuff size adapted to body weight and posture, as recommended by the manufacturer. The  $MAP_{iNIBP}$  measurement interval was set at 5 minutes.

The Nexfin cuff was placed at the intermediate phalanx, ipsi- or contralateral to the radial artery catheter, at the most accessible side.

To correct for hydrostatic pressure differences between the finger and the heart, the heart reference system (HRS™) is provided with the Nexfin device. Both the HRS™ and the arterial pressure transducer were located at the level of the right atrium.  $MAP_{invasive}$  and  $MAP_{iNIBP}$  data were recorded at a 1 second and 5 minute interval, respectively, using RugLoop II data-manager software (Demed, Temse, Belgium), connected to the anesthesia monitor (Philips MP70; Philips, Eindhoven, Netherlands).  $MAP_{cNIBP}$  and other hemodynamic data (heart rate, cardiac index, systemic vascular resistance index, dP/dT) were recorded in a beat-to-beat fashion on the Nexfin monitor. Values of  $MAP_{invasive}$ ,  $MAP_{iNIBP}$  and  $MAP_{cNIBP}$  were imported into Microsoft Excel 2010® (Microsoft, Redmond, WA) and synchronized. After graphical representation of these values, a visual inspection was performed to correct for obvious atypical values caused by artifacts (mostly resulting from blood sampling and NIBP cuff inflation).

### Statistical analysis

All statistics were performed using Microsoft Excel 2010® and PASW Statistics 18 (SPSS Inc, Chicago, USA). A 30-second running median with 1-second steps was calculated for  $MAP_{invasive}$  and  $MAP_{cNIBP}$ . Normality of continuous variables was assessed using the Kolmogorov-Smirnov test. Data were expressed as mean (SD), median (range) or number of patients (%). The distribution (median, 2.5<sup>th</sup> and 97.5<sup>th</sup> percentile) of the difference with  $MAP_{invasive}$  (either  $MAP_{cNIBP}$  or  $MAP_{iNIBP}$  minus  $MAP_{invasive}$ ) was plotted for the 30 minute time period. The Mann-Whitney U test was performed to test whether the difference in bias of both methods was significantly different. A modified Bland Altman analysis for repeated measurements<sup>13-15</sup> was performed for comparison of all data points of  $MAP_{cNIBP}$  with  $MAP_{invasive}$  and of  $MAP_{iNIBP}$  with  $MAP_{invasive}$  at a 5 minute time interval. In cases cuff inflation influenced continuous measurements, these variables were determined just before inflation of the cuff and correlated with the subsequent  $MAP_{iNIBP}$  value. Here, the bias (SD) is calculated together with the limits of agreement (LOA = the bias  $\pm$  1.96SD). As a measure of precision<sup>16</sup>, coefficients of error (CE) were calculated as the SD of the bias divided by the mean of measurements. Subsequently, percentage errors for  $MAP_{cNIBP}$  and  $MAP_{iNIBP}$  compared to  $MAP_{invasive}$  were calculated as:  $2.0 * CE * 100$ ; here CE is from either  $MAP_{cNIBP}$  or  $MAP_{iNIBP}$  bias.<sup>17</sup>

Currently, two guidelines apply to validation of blood pressure measurement by the Nexfin: one from the European Working Group for the Validation of Blood Pressure Measuring Devices (ESH criteria) and one from the Association for the Advancement of Medical Instrumentation (AAMI).<sup>18,19</sup> The requirements for validation by the ESH criteria are summarized in the legends of table 1.

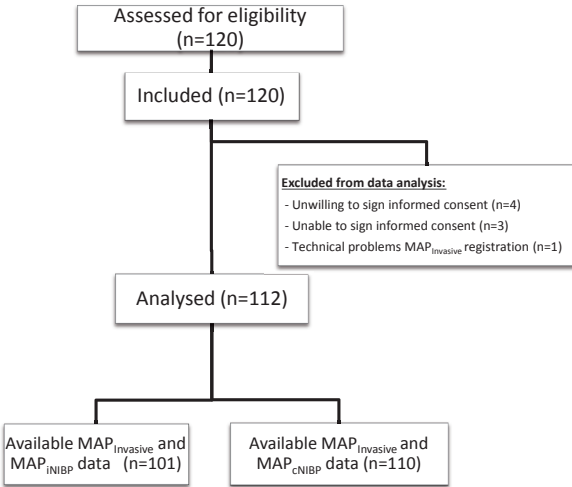
	Very accurate ( $< 5$ mmHg)	Slightly inaccurate ( $< 10$ mmHg)	Inaccurate ( $< 15$ mmHg)
Pass all three:	65%	81%	93%
Pass two of three:	73%	87%	96%

**Table 1:** Requirements for blood pressure measurement validation as set by the European Working Group for the Validation of Blood Pressure Measuring Devices (ESH criteria). Shown is the required minimal percentage of MAP measurements being either very accurate, slightly inaccurate, or inaccurate. In order to determine whether a device passes the ESH criteria, either two of three minimal accuracy requirements (step 1) or all three minimal accuracy requirements (step 2) should be achieved.

Furthermore, AAMI criteria consider a device acceptable if its estimated probability of tolerable error is at least 85%, suggesting that a predefined estimated sample mean error of 5 mmHg should have a concomitant standard deviation below 8 mmHg. Sample size calculation for our study was based on the AAMI criteria and was calculated in order to detect a mean difference of 5 mmHg. For an estimated SD of MAP values of 9 mmHg, a power of 98% and an alpha error of 0.05, at least 106 patients should be included. Therefore, we included 120 patients in total. Statistical significance level was assumed if  $p < 0.05$ .

### Results

A total of 120 patients were included (figure 1). Eight patients were excluded from data analysis because of unwillingness or inability to sign informed consent ( $n=7$ ) or technical reasons ( $n=1$ ). Of the 112 patients analyzed in total, 2 data sets could not be used for the comparison of MAP<sub>CNIBP</sub> with MAP<sub>invasive</sub> and 11 data sets could not be used for the comparison of MAP<sub>INIBP</sub> with MAP<sub>invasive</sub>, all because of technical difficulties with recording MAP<sub>CNIBP</sub> or MAP<sub>INIBP</sub> respectively.



**Figure 1:** Consort flow diagram.

Characteristics of the studied patients ( $n=112$ ) were normally distributed and are shown together with main hemodynamic variables in table 2.

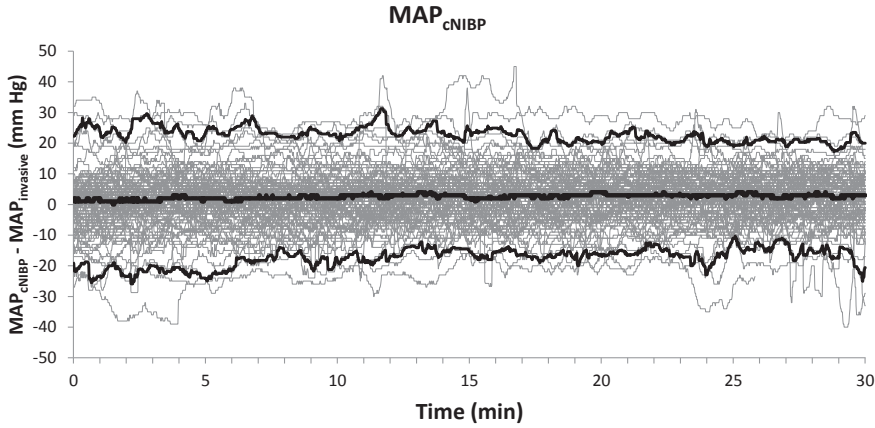
Age (years)	59 (13)
Weight (kg)	83 (19)
Height (cm)	175 (10)
ASA classification	
I	11 (9%)
II	67 (60%)
III	32 (29%)
IV	2 (2%)
Heart rate (beats $\text{min}^{-1}$ )	69 (12)
MAP <sub>invasive</sub> (mmHg)	82 (11)
Cardiac Index ( $\text{L min}^{-1} \text{m}^{-2}$ )	2.9 (0.7)
Systemic Vascular Resistance Index ( $\text{dynes sec}^{-1} \text{cm}^{-5} \text{m}^{-2}$ )	2398 (695)
dP/dT ( $\text{mmHg sec}^{-1}$ )	624 (238)

**Table 2:** Patient characteristics and main hemodynamic variables. Values are expressed as mean (SD) or as N (%) for categorical variables. ( $n=112$ )

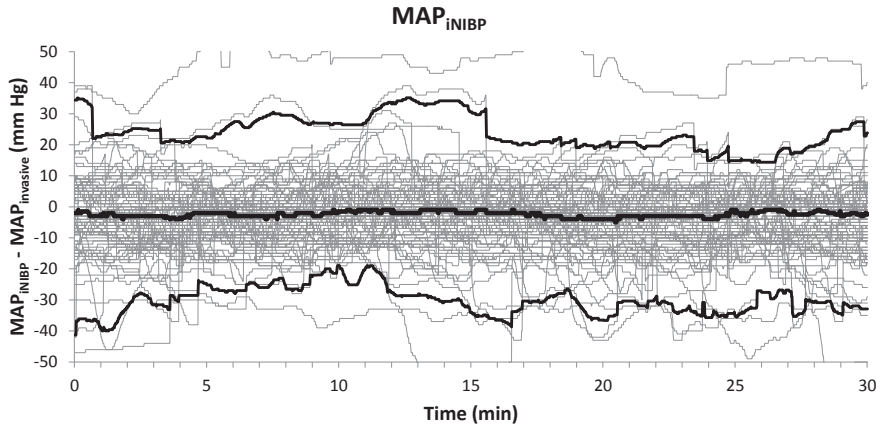


Figure 2A-B shows the individual differences with  $MAP_{invasive}$  values of  $MAP_{cNIBP}$  (A) and  $MAP_{iNIBP}$  measurements (B) for the 30-minute measurement period of all patients together with its median and concomitant 2.5<sup>th</sup> and 97.5<sup>th</sup> percentile.

**Figure 2A:**



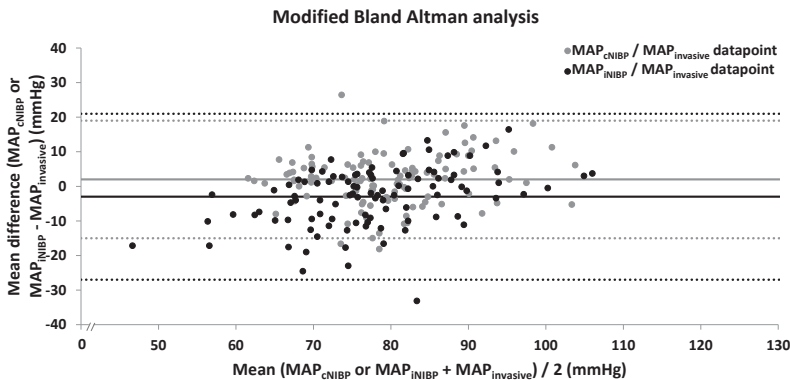
**Figure 2B:**



*Figure 2A-B: The evolution in individual patients of the differences with  $MAP_{invasive}$  of the continuous measurement of  $MAP_{cNIBP}$  (A) and the intermittent measurements of  $MAP_{iNIBP}$  (B) over the 30-minute period in mmHg. Individual patients (thin grey lines) and median values (middle thick line) are shown together with the 2.5<sup>th</sup> and 97.5<sup>th</sup> percentile (outer thick lines).*

The median difference (2.5<sup>th</sup> / 97.5<sup>th</sup> percentile) of  $MAP_{cNIBP}$  at the start of measurements was 1 mmHg (-13/8 mmHg) and was 3 mmHg (-8 /11 mmHg) after 30 minutes. The median difference of  $MAP_{iNIBP}$  was -2 mmHg (-18/14 mmHg) at the start of measurements and was -2 mmHg (-18/8 mmHg) after 30 minutes. For all data points, the bias of  $MAP_{cNIBP}$  was significantly different from that of  $MAP_{iNIBP}$  ( $p < 0.001$ , Mann-Whitney U test).

In figure 3 and table 3, the bias (SD) and LOA's, as derived from the modified Bland-Altman analysis for repeated measurements, are shown for the 30-minute time period with a time interval of 5 minutes. Also in table 3, coefficients of error (CE) and percentage errors for both  $MAP_{cNIBP}$  and  $MAP_{iNIBP}$  are shown.



**Figure 3:** Modified Bland-Altman plot for repeated measurements of the difference between  $MAP_{invasive}$  and either  $MAP_{cNIBP}$  or  $MAP_{iNIBP}$  against the mean of these measurements. The values given are calculated relative to the  $MAP_{invasive}$ . Horizontal dotted lines show the bias. Continuous horizontal lines show the limits of agreement ( $LOA = bias \pm 1.96SD$ ) for  $MAP_{cNIBP}$  (grey) and  $MAP_{iNIBP}$  (black).

The performance of both  $MAP_{cNIBP}$  and  $MAP_{iNIBP}$  measurement as an alternative for  $MAP_{invasive}$  is shown in table 1 for both steps of the ESH reliability criteria. Neither  $MAP_{cNIBP}$  nor  $MAP_{iNIBP}$  measurements succeeded to match any of these criteria. Both measurement methods also failed to meet the AAMI criteria (table 3)

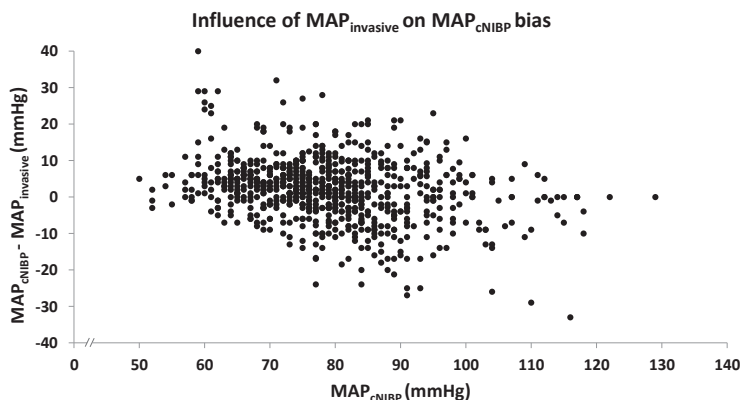
	Bias (SD) (mm Hg)	LOA (mmHg)	CE (%)	PE (%)
$MAP_{cNIBP}$	2 (9)	-15 / 19	11	22
$MAP_{iNIBP}$	-2 (12)	-26 / 21	16	32

**Table 3:** Modified Bland Altman analysis for repeated measurements. Shown is a comparison for all available data points of the agreement between either  $MAP_{iNIBP}$  ( $n=692$ ) or  $MAP_{cNIBP}$  ( $n=758$ ) with  $MAP_{invasive}$ . Shown is the bias (SD), lower and upper limits of agreement (LOA), the coefficients of error (CE) and percentage errors (PE) ( $n=765$ ).

#### *Influence of measurement side and absolute $MAP_{invasive}$ value on $MAP_{cNIBP}$ bias*

The Nexfin® cuff was attached to the index finger ipsilateral to the inserted radial artery catheter in 70 patients (63%), whereas it was attached to the contralateral side in 42 patients (37%). Modified Bland-Altman analysis for repeated measurements revealed no differences in agreement of  $MAP_{cNIBP}$  with  $MAP_{invasive}$  between both measurement sides: bias (SD) was 2 (9) mmHg (LOA: -16 / 20 mmHg) for ipsilateral and 2 (8) mmHg (LOA: -14 / 18mmHg) for contralateral measurements.

Figure 4 shows the influence of  $MAP_{invasive}$  on  $MAP_{cNIBP}$  accuracy. Values are shown for all data points ( $n=765$ ) in the 30-minute measurement period with an interval of 5 minutes. There was no correlation between the two variables.



**Figure 4:** Scatterplot showing the influence of the  $MAP_{invasive}$  value on  $MAP_{cNIBP}$  accuracy. Values are shown for data points ( $n=765$ ) in the 30-minute measurement period with an interval of 5 minutes.

## Discussion

The agreement of the Nexfin device with invasive blood pressure measurement as a gold standard has been studied in several recent studies, with varying results. However, much as replacement of invasive by noninvasive measurement has important advantages, most patients undergoing anesthesia are monitored in a noninvasive fashion, and may benefit from accurate and precise *continuous* noninvasive monitoring. To the best of our knowledge this is the first study investigating the potential benefit of the Nexfin to monitor blood pressure for these patients.

In the current study in patients under general anesthesia, the main purpose was to quantify the accuracy and precision of continuous noninvasive mean arterial blood pressure measurement using the Nexfin device ( $MAP_{cNIBP}$ ) and using conventional intermittent cuff oscillometry ( $MAP_{iNIBP}$ ), comparing both methods to the gold standard, i.e. continuous invasive measurement of mean arterial blood pressure ( $MAP_{invasive}$ ). Only periods of stable hemodynamic conditions were recorded and included for further analysis.

In this phase, the Nexfin-derived  $MAP_{cNIBP}$  showed an agreement with invasive measurements which was not inferior to the agreement of automated cuff oscillometry derived  $MAP_{iNIBP}$ . This suggests that this method is at least a valuable adjunct to measure MAP and might even be used as an alternative to  $MAP_{iNIBP}$  in patients undergoing anesthesia. We observed however that both  $MAP_{iNIBP}$  and  $MAP_{cNIBP}$  showed some imprecision with respect to invasive mean arterial blood pressure measurement ( $MAP_{invasive}$ ) and that both methods failed to meet the AAMI criteria as well as the ESH criteria for blood pressure measurement validation.

The accuracy of Nexfin-derived  $MAP_{cNIBP}$  measurements has been studied in a number of previous studies<sup>10-12,20-23</sup> and showed close correlations with  $MAP_{invasive}$  in patients undergoing cardiothoracic surgery<sup>11</sup>, and was considered reliable enough to replace invasive arterial pressure monitoring in

most patients.<sup>24</sup> MAP<sub>cNIBP</sub> and MAP<sub>iNIBP</sub> accuracy have until now only been compared in awake - non-anaesthetized – patients, and in these studies, they were not compared to any gold standard.

Studies comparing MAP<sub>cNIBP</sub> with MAP<sub>iNIBP</sub> in supine patients<sup>25</sup>, in acutely ill patients at an emergency department<sup>24</sup> or in pregnant women for longitudinal tracking of blood pressure<sup>26</sup> or in patients during autonomic function testing<sup>27</sup>, demonstrated adequate accuracies.

We however did not investigate the relationship between MAP<sub>cNIBP</sub> and MAP<sub>iNIBP</sub> measurements as in our opinion it is more relevant – in patients receiving (general) anesthesia – to directly compare both MAP<sub>cNIBP</sub> and MAP<sub>iNIBP</sub> measurements with the gold standard of continuous invasive MAP measurement (MAP<sub>invasive</sub>). Surprisingly, we found that both noninvasive measurement methods failed to meet the AAMI criteria because the precision – as an indication of measurement reproducibility – exceeded the pre-defined precision of 5 mmHg. Nevertheless, MAP<sub>cNIBP</sub> values were more closely related to MAP<sub>invasive</sub> values than the MAP<sub>iNIBP</sub> values, which was also true for the agreement data provided in tables 1 and 3. While statistically significant, the small absolute difference does not entail a clinically significant superior accuracy. There are, up to our knowledge, no other studies in which the accuracy of both MAP<sub>cNIBP</sub> and MAP<sub>iNIBP</sub> measurements were compared with MAP<sub>invasive</sub> measurements and therefore these findings require confirmation in future studies, particularly in conditions of hemodynamic instability and during vasopressor use.

A second point of major clinical importance is that while the difference in accuracy of both noninvasive methods is small and arguably not clinically significant, MAP<sub>cNIBP</sub> monitoring has the obvious advantage of providing MAP measurements both faster and in a continuous “beat-to-beat” fashion. In this view, although inevitably less accurate than MAP<sub>invasive</sub>, showing non-inferiority of absolute measurement of the MAP<sub>cNIBP</sub> relative to MAP<sub>iNIBP</sub> would be sufficient to advocate its use.

As pointed out in a recent study<sup>28</sup>, MAP<sub>cNIBP</sub> was able to detect significantly more periods of hypo- and hypertension in patients undergoing surgery compared to the use of MAP<sub>iNIBP</sub> monitoring. Additionally, the Nexfin device can also obtain flow-based hemodynamic variables such as cardiac output, although reports on the accuracy of these variables are sparse. Since MAP<sub>cNIBP</sub> is acquired at the finger, and the MAP<sub>invasive</sub> at the radial artery, while MAP<sub>iNIBP</sub> is measured at the brachial level, one may ask whether the reported superior agreement with invasive measurements is merely a consequence of the reference point. The Nexfin algorithm however performs a waveform transformation to reconstruct the arterial waveform and values, and therefore MAP<sub>cNIBP</sub> as well as MAP<sub>iNIBP</sub> values should be considered brachial MAP. In addition, since the higher errors in MAP<sub>iNIBP</sub> consist of overestimations as well as underestimations (fig 2), a difference in reference point is an unlikely reason for the divergent accuracy.

Still, non-inferiority of MAP<sub>cNIBP</sub> compared to MAP<sub>iNIBP</sub> does not necessarily result in improved patient outcome, but a faster diagnosis<sup>29</sup> implicates a significant potential for improved patient monitoring. An additional advantage is likely in patients where brachial measurements may be difficult such as obese patients or patients with brachial injuries or dialysis shunts. However, it has to be shown if the additional costs of measuring MAP<sub>cNIBP</sub> justify the benefits of its use described above, also in view of a recent change in the distributor of the device.

#### *Study limitations:*

All measurements were performed in patients at arbitrary moments during general anesthesia. The most important limitation therefore is that during these observation periods, no particularly considerable changes in blood pressure occurred and therefore the accuracy and precision of both MAP<sub>cNIBP</sub> and MAP<sub>iNIBP</sub> during substantial variations in blood pressure cannot be answered by this study. It has been demonstrated that the use of continuous noninvasive measurements decreases

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the total time of hypotension or hypertension during anesthesia significantly, but the accuracy of either assessments compared to a gold standard was not investigated in that study.<sup>30</sup>

Secondly, our measurements took place in patients with  $\text{MAP}_{\text{invasive}}$  at randomly selected moments during anesthesia. We did not specifically analyze the influence of changes in vascular tone, e.g. induced by changes in temperature or use of vasoactive drugs. This is, however, in accordance with normal clinical practice where reliability of  $\text{MAP}_{\text{cNIBP}}$  may also be dependent on a variety of physiological conditions. Although the Physiocal algorithm of the Nexfin monitor is developed to compensate for any changes in vascular tone due to peripheral hypothermia or other induced changes in local perfusion, we may not exclude a decrease in accuracy of finger-based methods in such cases. Therefore, our conclusions are only valid for normothermic, hemodynamically stable patients not requiring (high doses of) vasoactive medication.

It is well known that pulse-oximetry becomes less accurate in case of hyperpigmentation, low blood oxygen saturation or certain intoxications because pulse-oximetry is based on differential absorption of two distinct wavelengths. The plethysmographic measurement used for the volume clamp method, however, does not rely on such delicately distinct wavelength absorptions (it uses 1 wavelength only) and is therefore very unlikely to be less reliable in such circumstances, although no reports have confirmed this yet.

Despite the reliability of  $\text{MAP}_{\text{cNIBP}}$  compared to  $\text{MAP}_{\text{inNIBP}}$  our results also show that the agreement of  $\text{MAP}_{\text{cNIBP}}$  with  $\text{MAP}_{\text{invasive}}$  is not sufficient to advocate replacing  $\text{MAP}_{\text{invasive}}$  in any case. Therefore, high-risk patients undergoing major procedures, i.e. conditions where hypothermia or high vasopressor need may occur, will still require invasive MAP monitoring for most reliable blood pressure monitoring and arterial blood sampling.

Furthermore, insufflation of the  $\text{MAP}_{\text{inNIBP}}$  cuff is known to induce alterations in the vascular compliance due to endothelial activation and vasodilation. Our previous research demonstrates a sustained influence on distal limb physiology for several minutes after intermittent  $\text{MAP}_{\text{inNIBP}}$  cuff insufflation.<sup>31</sup> It is still subject of debate whether these microvascular changes are induced by ischemia, congestion, or other physiological phenomena, but it is conceivable that these local changes may influence the compliance of the vascular wall and therefore the accuracy of the  $\text{MAP}_{\text{cNIBP}}$  measurements. Contrarily, inter-arm anatomical differences can also cause different blood pressure readings.<sup>32</sup> Therefore, we measured  $\text{MAP}_{\text{cNIBP}}$  either ipsilaterally and contralaterally with regard to  $\text{MAP}_{\text{invasive}}$ . Since there was no blinded randomization on this matter, this may have influenced our results. However, a subanalysis comparing data received from the ipsilateral versus contralateral side did not reveal any significant differences (data not shown). Hence, we decided to group all data without further differentiating the side of  $\text{MAP}_{\text{cNIBP}}$  measurement.

Finally, all analysis was performed on MAP values, since these are most commonly used in comparing different monitoring devices<sup>33</sup> and also for guiding therapy. Comparison of systolic blood pressure values may vary somewhat from our results, although these were not reported for conciseness.

**Conclusion:** This study shows that in a hemodynamically stable phase in patients under general anesthesia, the agreement with invasive mean arterial pressure measurements of Nexfin-derived  $\text{MAP}_{\text{cNIBP}}$  was found to be non-inferior to conventional  $\text{MAP}_{\text{inNIBP}}$  measurements. Although influence on outcome was not investigated, this study demonstrates that  $\text{MAP}_{\text{cNIBP}}$  has significant potential to improve patient monitoring in hemodynamically stable patients undergoing anesthesia where  $\text{MAP}_{\text{inNIBP}}$  is at present being clinically used.

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